Conclusion: LV regional wall motion appears to be of prognostic importance and is improved by carvedilol therapy. These data provide further support for the beneficial effects of beta-blockade in patients with heart failure.

9:30

727-5 The Hemodynamic and Neurohumoral Effects of Moxonidine, a Sympathetic Inhibitor, in Congestive Heart Failure

K. Dickstein, U. Köpp, C. Manhenke, T. Aarsland, F. Waagstein, R. Mobini, J. McNay. *Central Hospital in Rogaland, Stavanger, Norway*

Background: Congestive heart failure is characterized by a pathologically elevated peripheral vascular resistance and elevated noradrenaline (NA) concentration. Chronic adrenergic stimulation may have deleterious effects on the cardiovascular system. Moxonidine (MOX), via imidazoline receptor agonism, reduces central sympathetic outflow and circulating NA.

Methods: This study evaluated the neurohumoral and hemodynamic effects of oral MOX in 30 patients (mean age 66 ± 10 years) with NYHA class III congestive heart failure. Mean ejection fraction was 28 ± 5%, mean pulmonary capillary wedge pressure was 25 ± 7 mmHg and mean NA was 505 ± 302 pg/ml. Patients underwent 12 hour invasive hemodynamic monitoring following blinded randomization to placebo (n = 12), 0.4 or 0.6 mg MOX (n = 18 combined). All other vasoactive agents were withheld on the study day.

Results:

Changes from baseline at 3 and 6 hours post dose.

	MAP (mmHg)	PCWP (mmHg)	SVR (dynes·sec·cm^{-5})	NA (pg/ml)
3 hours Placebo	−0.6	−2.5	−49	8
MOX	−13.3*	−4.9*	−154*	−165**
6 hours Placebo	0.3	−2.1	4	−11
MOX	−12.6*	−4.1*	−216*	−186**

*p < 0.01, ** p< 0.005. MAP = Mean Arterial Pressure, PCWP = Pulmonary Capillary Wedge Pressure, SVR = Systemic Vascular Resistance, NA = Noradrenaline.

Conclusions: MOX was well tolerated and resulted in a modest, dose-dependent vasodilator response. Substantial reductions in NA were observed. These data suggest that moxonidine therapy may reduce vascular resistance and improve the hemodynamic profile in patients with CHF.

9:45

727-6 The Preventive Effect of Ascorbate on Nitrate Tolerance in Patients with Congestive Heart Failure

H. Watanabe, M. Kakihana [1], S. Ohtsuka, Y. Sugishita. *University of Tsukuba, Tsukuba, Japan,* [1] *Ibaraki Prefectural University of Health Sciences, Ibaraki, Japan*

The attenuation of intracellular cGMP has been known as an important mechanism of nitrate tolerance. Recently, it was reported that increased superoxide reduced the production of cGMP due to inactivation of guanylate cyclase. This study was designed to investigate the effects of ascorbate, an antioxidant of superoxide, on nitrate tolerance in patients with congestive heart failure. Twelve patients with chronic heart failure admitted to our hospital for worsening symptoms were randomized to receive either an intravenous infusion of nitroglycerin (NTG) alone (1.5 μg/kg/min [NTG group, n = 6]) or concomitantly with intravenous ascorbate (55 μg/kg/min [NTG + Vit C group, n = 6]). Hemodynamic parameters and platelet cGMP were measured serially at the baseline, 6, 12, and 18 hours after the infusion of NTG alone or NTG concomitantly with ascorbate. At the baseline, mean pulmonary artery pressure (PA, mmHg), mean pulmonary capillary wedge pressure (PCWP, mmHg) and platelet cGMP (pmol/10^9 PLT) level were comparable in the two groups. At 6 hours, PA and PCWP were significantly decreased (NTG group, PA: 48 ± 3 to 26 ± 3, p < 0.05; PCWP: 25 ± 4 to 15 ± 2, p < 0.05; NTG + Vit C group, PA: 49 ± 3 to 26 ± 3, p < 0.05; PCWP: 24 ± 4 to 16 ± 3, p < 0.05), and platelet cGMP was significantly elevated (NTG group, 0.76 ± 0.12 to 2.42 ± 0.24, p < 0.05; NTG + Vit C group, 0.71 ± 0.16 to 2.26 ± 0.37, p < 0.05). At 12 hours, the effects of NTG on PA, PCWP and platelet cGMP were maintained. However, at 18 hours, in the NTG group, PA and PCWP were elevated (PA: 44 ± 3, PCWP: 23 ± 3) and platelet cGMP was decreased (0.85 ± 0.20). In contrast, in the NTG + Vit C group, NTG effects in PA (31 ± 4), PCWP (17 ± 4) and platelet cGMP (2.49 ± 0.42) were maintained throughout this study.

Conclusions: These results indicated that the concomitant use of ascorbate may prevent the development of nitrate tolerance in patients with heart failure treated with NTG.

TUESDAY ORAL

728 Stents: New Devices and Techniques

Tuesday, March 18, 1997, 8:30 a.m.–10:00 a.m.
Anaheim Hilton and Towers, Pacific C

8:30

728-1 A Multicenter Randomized Trial Comparing the Second Generation Gianturco-Roubin (GR II™) and the Palmaz-Schatz Coronary Stents

Multicenter GRII™ Investigator Group, M. Leon. *Washington Hospital Center, Washington, DC, USA*

Direct comparisons of clinical outcomes for two stent designs in a randomized trial eliminates the confounding influences of differing patient selection criteria and indications for use. The second generation Gianturco-Roubin (GRII™) balloon-expandable coronary stent (20 and 40 mm lengths), with a flat wire clamshell design, low profile, and radio-opaque end-markers is being compared to the commercially available Palmaz-Schatz (PS) tubular slotted (15 mm length). Enrollment criteria include patients undergoing successful elective PTCA of *de novo* lesions with reference vessel size 3–4 mm and lesion length <30 mm. For longer lesions which could not be covered by a single 15 mm PS or 20 mm GRII™ stent, two PS or two 20 mm GRII™ or one 40 mm GRII™ stent is permitted. Patients with recent MI (<7 days), LVEF < 35%, poor distal run-off, or residual thrombus in the target lesion are excluded. A sample size of 750 patients (375 per arm) was chosen to demonstrate equivalent rates of freedom from major cardiac events (death, Q-MI, CABG, repeat PTCA) @ 9 months follow-up (primary end-point). Other important endpoints include quantitative angiographic analyses (follow-up minimum lumen diameter and binary restenosis) @ 9 months, in-hospital procedure success and major clinical events, and 30-day major clinical events. Since January 1996, 31 investigator sites have enrolled 595 patients (302 GRII™ and 293 PS) and enrollment is nearing completion. *Comparative analyses of procedural results (including quantitative angiographic findings), in-hospital major clinical events, and 30-day clinical outcomes will be presented.*

8:45

728-2 BENESTENT-II Trial – Final results of Visit I: A 15-Day Follow-Up

V. Legrand, P.W. Serruys, H. Emanuelsson, J. Fajadet, M. Haude, S. Klugmann, F. Bår, F. Fernández-Avilés, H. Suryapranata, M.A. Morel. *Thoraxcenter, Rotterdam, NL*

The BENESTENT-II Trial is a randomized trial comparing the outcome after balloon angioplasty, with the effect of Heparin-coated Palmaz-Schatz stent (10, 15 and 20 mm long with one or multiple helicoidal articulations) on the long-term effect of Major Adverse Cardiac Events (MACE: Death, MI, Target Lesion Revascularisation [TLR]), in patients with stable or stabilized unstable angina pectoris with one or more de novo lesions. The secondary objectives are to assess the Cost-effectiveness and the restenosis rate. To that purpose a 1:1 sub-randomization to either clinical or angiographic follow-up was carried out. Concomitant medications consist of Aspirin (≥100 mg) and Ticlopidin (250 mg, 30 days) in the stent group. Between August 28th '95 and March 7th '96, 827 patients were randomized to either treatment with stent (414) or balloon (413). Forty-three percent of the patients had unstable angina, 51% stable and 6% silent ischemia. 6% underwent multiple lesion treatment. 54% of the lesions were B2 lesions (AHA/ACC). In the balloon group 13.4% of the patients received a bail-out stent according to preset stringent criteria: procedural success is 97% in the stent group and 86% in the balloon group according to the actual allocation protocol. The hospital stay in the stent group was 2.4 days vs 2.1 days in the balloon group. Subacute occlusion was observed in one patient in the stent group vs 7 patients in the balloon group. Bleeding and vascular complications in both groups were low (0.7 vs 0.5%). At 15 days Fup, the total count of MACE amounts to 4.3% (*n = 18*) in the stent group vs 6.5% (*n = 27*) in the balloon group. Sixteen patients in the stent group (3.9%) vs 18 (4.4%) in the balloon group have at least one event. In 10 patients the Ticlopidin was stopped because of adverse reaction, but no leucopenia, neutropenia, thrombocytopenia was observed. The MLD achieved in the stent group was 2.69 mm vs 2.15 mm in the balloon group. Based on the acute QCA results and applying a validated multivariate analysis derived from Benestent-I, we expect significant differences in Restenosis rate (13% vs 28%) and in event rates at follow-up. It remains to be demonstrated whether elective stenting will be at long-term more cost-effective than balloon.